Letters

On the desirability of models for inferring genome phylogenies

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Genomes are clearly suited for inferring common ancestry and for understanding ancestor–descendent relationships and interspecies gene transfer. Genomic evolutionary models can tell us a great deal about the processes that drive genome evolution, the mutational and selective pressures that lead to the genesis of biochemical pathways and operons, and the nature and extent of lateral gene transfer (LGT). Simultaneously, a robust phylogeny can be constructed that depicts the evolutionary relationships of the organisms in which the genomes are found.

Several approaches have been employed to infer species phylogenies at the genome level. In general terms, these can be divided into *ad hoc* summary statistics based on genome content, the use of concatenated alignments and the use of consensus methods (i.e. phylogenetic supertrees [1]).

The basic premise of methods based on summary statistics is that genomes are compared and a gene content matrix is compiled. Then, either a distance is estimated between all pairs of taxa and entered into a distance matrix that is summarized using a clustering algorithm, or a dendrogram is inferred using maximum parsimony. This is usually referred to as the species phylogeny. The principal difference between this approach and the approaches that use concatenated alignments or supertrees is that information concerning homolog interrelationships is not used. Presence or absence of homologs is the only information that is scored, and this approach can be considered *ad hoc* in the sense that the methods are applied uniformly to all datasets and, therefore, the assumptions are not informed by the data themselves.

Unsurprisingly, the results of using summary statistics have been variable. Although many methods have recovered groups that seem sensible and have support from external biochemical or morphological data, there have been cases in which the inferred trees are unusual [2].

For example, the haloarchaea are a group of halophilic Archaea, long taken to be members of the Euryarchaeota. Wolf *et al.* [2] and Korbel *et al.* [3] placed this taxon at the base of the Archaea. In the figures of Henz *et al.* [4], this taxon was placed among the Bacteria in one instance, within the Euryarchaeota in a second example and as the deepest-branching Archaeon in a third example. Dutilh *et al.* [5] point out that the correct placement of the haloarchaea is within the Euryarchaeota and that previous methods placed this taxon erroneously as a deep-branching Archaeon. This erroneous placement is likely to be due to the large number of bacterial genes present in the haloarchaea [6]. The haloarchaea are, therefore, pulled to a position that is intermediate between the two groups from which the haloarchaea genes came. The data violate the *ad hoc* assumptions of the methods. Problems of this nature argue for the development of explicit genome evolutionary models.

Evolutionary models are statements concerning how it is thought that evolution has occurred [7]. If a model were correct, the inferred distances between two genomes would be accurate and would provide consistent estimates of the topology of the resulting phylogeny. The most desirable properties of these models are explicitness when describing the evolutionary process, realism or plausibility of the assumptions contained in the models and clarity in the interpretation of the output [8]. Usually, models are derived in a maximum likelihood framework in which the model consists of the phylogenetic tree of the genomes and the process underlying their evolution [9]. However, even when alternative models are not tested or lengthy computational optimization is not performed, an explicit model of evolution can still be assumed in calculations [10].

A realistic model of genome evolution must, as a minimum, deal with gene duplication and loss, in addition to acquisition of genes by LGT. This is not to say that all parameters are necessary for all analyses. When models differ in their numbers of free parameters and are nested, a likelihood ratio test can be used to choose the most appropriate parameter.

Gu and Zhang [11] describe a model called the extended genome content distance. This model uses the number of homologs (0, 1 or >1) to derive the genome distance. The model does not take account of horizontal gene transfer and, as a result, the authors report a position for the haloarchaea that is the same as the much simpler method of Korbel *et al.* [3]. A model has also been developed that deals with LGT, albeit in a slightly different setting [12]. Nonetheless, the development of explicit model-based approaches is to be welcomed as a useful step towards the understanding of genome evolution.

When the genomic age began, it was assumed that the huge increase in the amount of available data would result in more-accurate phylogenies. Instead, the extent of apparent genome plasticity has fueled a passionate debate

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Available online 3 November 2005

concerning prokaryotic evolution. Sensible genome models that provide information about phylogeny and the process of evolution should be a goal for genomics and systematics.

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0966-842X/$ - see front matter
doi:10.1016/j.tim.2005.10.006

Bifunctional TatA subunits in minimal Tat protein translocases

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Bacteria export numerous proteins across the cytoplasmic membrane into the periplasmic space and outer membrane (Gram-negative species) or the extracellular milieu (Gram-positive species). In most bacteria, the bulk of this protein traffic is mediated by the general secretory (Sec) pathway, which requires 'threading' of transported proteins through a membrane-bound Sec translocon in an unfolded state. Upon membrane translocation, exported proteins fold into their final conformation. Recently, a second pathway for protein export has been identified: the twin-arginine translocation (Tat) system, which derives its name from the twin-arginine (RR) motif that is an essential determinant in the signal peptide of Tat-system substrates. This pathway is conserved in Bacteria, Archaea and chloroplast thylakoids. In marked contrast to the Sec system, the Tat system translocates globular proteins in a folded state. This striking characteristic of Tat systems has attracted wide interest and is discussed in excellent reviews by Palmer *et al.* [1], and Robinson and Bolhuis [2].

In *Escherichia coli* and chloroplast thylakoids, an active Tat system canonically requires the presence of three membrane-bound subunits: TatA, TatB and TatC. Absence of one of these subunits results in impaired function of the Tat machinery, at least with respect to the export of known authentic substrates. The currently accepted view is that, in complex, TatB and TatC serve in RR-signal-peptide reception, whereas, in complex with multiple TatA subunits, they form protein-conducting channels [3,4]. Association of TatA with complexed TatB and TatC subunits requires a functional precursor and the ΔpH component of the proton-motive force [3,4]. TatA subunits are likely to be recruited by TatB [1]. Here, we highlight the novel finding that TatA has the intrinsic capability to complement for the essential TatB subunit.

Phylogenetic analyses have shown that many bacteria and archaea contain genes that encode multiple TatA-, TatB-, and TatC-like proteins. Known TatA and TatB proteins show limited amino acid sequence similarity (Figure 1). Much clearer similarities between TatA and TatB proteins are, however, observed at the level of their predicted membrane topologies and structures (Figure 2a). A distinctive feature of these proteins is the presence of a conserved motif at the hinge between the transmembrane segment and the amphipathic cytoplasmic helix: Phe-Gly (FG) in TatA and Gly-Pro

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Available online 21 November 2005